PREFRONTAL LEUCOTOMY

(A Review)

By E. Cunningham Dax, M.B., B.S., B.Sc.(Lond.), D.P.M.,
R. K. Freudenberg, M.D., D.P.M.,   F. Reitman, M.D., D.P.M.,
E. J. Radley-Smith, M.S., F.R.C.S.

Netherne Hospital, Coulsdon, Surrey

Introduction

During the past 20 years a number of physical methods of treatment have been introduced on a large scale for the alleviation of mental illness. Despite much research the successes of insulin treatment in schizophrenia, convulsion therapy in depressive states and prolonged narcosis in emotional disturbance still remain unexplained even to the point of their still being empirical. Moreover, none of these methods can be expected to produce any radical changes in the personality of the patient, which means that, although the recovery from an attack of illness may be effected by these methods when it had hitherto been unlikely or a remission of a better quality than was seen in the past may be obtained, the susceptibility of the patient to his particular type of illness still remains.

The introduction of the operation of prefrontal leucotomy by Egas Moniz in 1935 offered opportunities for the development of a more radical form of mental treatment. The section of a portion of the white matter in the frontal lobes of the brain might be expected to result not only in a modification of certain thought processes but also in a changed personality perhaps even to the extent of remedying past inadequacies although the possible sacrifice of other cerebral functions as the result of the injury must be weighed in the balance. The anatomical, physiological, clinical, psychological and pathological investigations to which the operation leads should be of very great importance both towards the elucidation of the basis of mental illness and in the expansion of the knowledge of cerebral localization and function. It is not, therefore, surprising that the literature on the operation should have grown to large proportions since the publication of the initial papers and Freeman and Watts' book in 1942 on the operation, its history and the functions of the frontal lobes. Much of the writing has dealt with modifications of the original operation, the indications for its use and the results obtained and these will be discussed in more detail in the course of the paper. It may, however, be useful to introduce the sections which follow by a brief summary of the present position.

Moniz had been working upon the function of the frontal lobes in mental disorder for some two years before the International Neurological Congress of 1935 at which the work of Fulton, Jacobson and others was recorded. Their findings, which showed that frontal lobe lesions would modify experimentally induced neuroses in animals, when incorporated with his own studies induced Moniz, together with Lima, to perform their first leucotomy operations towards the end of the year by injecting absolute alcohol into the frontal lobes through an approach 3 cm. on either side of the midline of the skull.

Since that time the operation has been modified by entering the skull in the fronto-parietal region, in the temporal fossa, through the roof of the orbit or by turning back a frontal flap. The destruction of the brain matter has been effected with alcohol, wire and rotating leucotomes, and sharp and blunt instruments of various shapes and sizes. The extent of the incisions have varied from localized lesions of small size in the white matter above the orbital cortex to a complete section of the white matter in the place of the coronal suture or from the removal of small areas of cortex to a bilateral partial lobectomy. . The section of the white matter has been made in vertical planes from near the tips of the frontal lobes to a centimetre or more behind the anterior extremities of the lateral ventricles, whilst horizontal and oblique incisions and even temporal and parietal leucotomies have been performed. Successes have been obtained by its use in such widely separated complaints as intractable pain, epilepsy and homosexuality, but the percentages of patients who have improved have varied very greatly.

It is, therefore, becoming increasingly difficult to summarize the position in regard to the operation. At present the method introduced by Free-
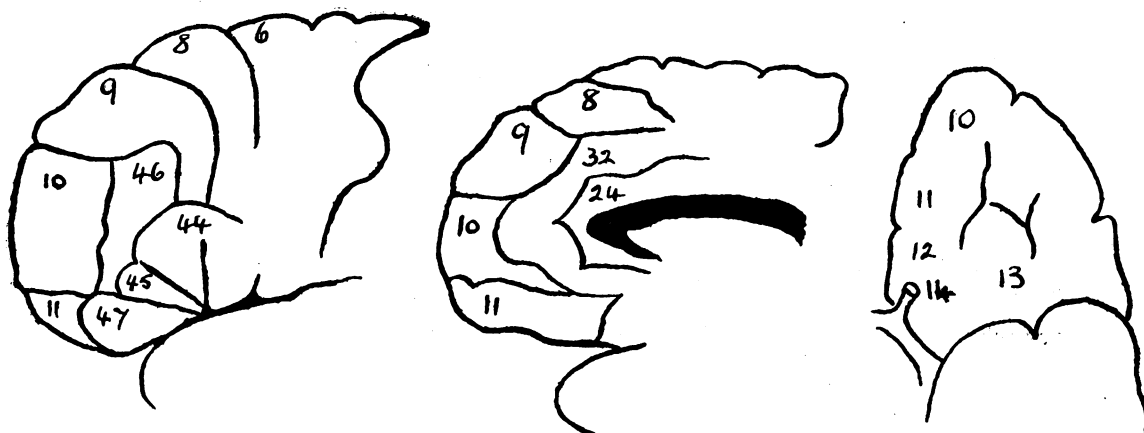
FIG. 1.—Diagram showing the cortical areas of the prefrontal lobes (mainly after Brodman).

man and Watts is the most popular, in which as much white matter as possible is incised in a vertical plane directly in front of the tips of the lateral ventricles through an opening 3 cm. behind the orbital margin and 6 cm. above the zygoma, by means of a blunt instrument. The cases which show most benefit from the operation are obsessionals and melancholics, and the symptoms which are most easily eliminated are tension, depression, introspection and excessive deliberation. Most writers agree that the operation should not be performed until other appropriate forms of treatment have been given a fair trial, that behaviour disorders in the psychoses often respond favourably and that a considerable number of chronic schizophrenics derive benefit from its use. The future of the operation must obviously lie in attempting to produce the maximum effect but at the same time the minimum cerebral damage.

Anatomy and Physiology

The present position as regards the knowledge of the anatomy of the frontal lobes of the brain has recently been reviewed by Le Gros Clark (1948). The frontal lobe is understood to be that part of the brain which is situated anterior to the motor and premotor cortex consisting of areas 8—12, 24, 32 and 44—47 of Brodman (Fig. 1). The boundaries of these areas are variable and not easy to define. This introduces an important difficulty in the study of the functions of these areas especially in connection with prefrontal leucotomy since it is a blind operation. In an attempt to produce more localized lesions single gyri have been excised recently by some workers and for this purpose the frontal lobe is exposed by a large bone flap. Because of the variability of the convolutional pattern it is very difficult to be certain, even under these conditions, as to which area has been excised.

Only detailed anatomical studies of leucotomized or gyrectomized brains from patients who died some time after the operation can lead to reliable information in this respect.

Le Gros Clark (1948) states that the frontal lobes should now primarily be regarded as an afferent projection area. They can in this way be compared with the visual and auditory cortex.

Von Bonin (1941) showed that the frontal lobes do not exhibit as much progressive enlargement in the ascending phylogenetic scale as the parietal and temporal lobes. This makes it doubtful whether the frontal lobes are really the seat of the highest mental integrative function. Parts of the temporal cortex are a more definite association area as association systems are received there from many other areas of the cortex. These parts have, together with the insular cortex, the special characteristics of having no afferent projection systems from the thalamus, in direct contrast to the connections of the frontal lobes.

The function of the different areas of the frontal cortex is still incompletely understood. Walker (1940) has introduced a further sub-division of the areas of the visual cortex leading to a modification of the Brodman scheme. He describes an area 14 on the medial and chiasmal part of the orbital surface and area 13 lying laterally to it. Area 13 is correlated with autonomic function. Bailey and Sweet (1940) found that stimulation of this area inhibits gastric peristalsis as well as respiration. Recent experimental work has shown that the frequency rate of stimulation is of great importance for the type of response seen. Bilateral removal of area 13 causes a fall in blood pressure and a rise in skin temperature leading to increased heat loss. Stimulation of the vagus produces spikes in neuronographic records from area 13 which is therefore considered to be a cortical area

related to parasympathetic function. Autonomic disturbances following prefrontal leucotomy have been studied by Reitman (1945). He stimulated the autonomic system in pre- and post-operative cases and noted alterations in the autonomic homeostasis. He also registered post-operative alterations in the gastric vagus juice secretion (1947). Rinkel (1947) found, by studying autonomic effects on the circulatory system, that after lobotomy the autonomic equilibrium is established at a new level. It appears, however, from Fulton's reports that one is only permitted to draw general conclusions after such clinical studies. Hemphill (1946) reported an increase on the 17-ketosteroid excretion following leucotomy and believed that a fronto-hypothalamic-pituitary circuit was influenced by leucotomy. Apart from the four quoted papers, little is reported on physiological investigations in connection with leucotomy. Grenville and Last (1947) found a marked delta activity arising from the part of the brain which lies rostral to the incision. This finding has not been reinvestigated by other authors. The hyperactivity observed after extirpation bilaterally of area 13 or after interruption of its projection fibres is especially marked (Ruch and Shenkin, 1943). Preoptic extirpation of area 14 leads to a state of rage according to Fulton and Ingram (1929). (See also later Reitman.)

Experiments involving stimulation of areas 9 and 10 have so far shown no positive results, but Jacobson (1943) found in monkeys and chimpanzees that removal of parts of area 9 and 10 was responsible for disturbances in recent memory. Most experimental studies on behaviour changes were undertaken after removal of the whole prefrontal cortex (Fulton, 1943). Monkeys and chimpanzees are more restless and distractable following extirpation of the prefrontal cortex, they exhibit a fatuous equanimity of spirit, their capacity for recall is impaired and they attach more importance to immediate sensory experiences. The animal lives in a perpetual present. Removal of the parietal and occipital lobes seems to have no such effect (Jacobson and Elder, 1936 ; Rylander, 1947). Leucotomies in different planes and lobotomies have recently been carried out in the macaque monkey by Freudenberg, Glees, Obrador, Foss and Williams (1947). Decrease in aggressiveness was most pronounced after complete lobotomy in the vertical plane. Motor activity was increased by lower orbital cuts in the vertical and horizontal planes.

The association tracts of the frontal lobes are insufficiently known but according to Le Gros Clark it can be assumed that short interconnections exist between different frontal areas. Long association tracts connect area 8 and 18, there is also a callosal connection from area 8 to 18 on the opposite side. This is unusual as most callosal fibres only connect with the same areas in the opposite hemisphere. Bailey, von Bonin and Davies (1944) have shown that area 31 and 32 receive afferent connections from all suppressor areas (2, 4S, 8, 19, 24) and no association fibres from other cortical areas. Area 32 also gives off afferent fibres connecting it with the suppressor areas ; this area, therefore, seems intimately concerned with the function of the entire cortex.

Connections of the Dorsomedial Nucleus of the Thalamus (D.M.N.)

The dorsomedial nucleus was found to degenerate after leucotomy. A description of its connections is, therefore, necessary in this respect. Clark and Boggon (1933) showed in experimental studies that a large part of the frontal lobe is a projection area for the D.M.N. Walker (1938) has shown connections of the D.M.N. with the frontal cortex in the macaque monkey. Mettler (1947), Meyer and McLardy (1947) conclude that the pars magnocellularis of the D.M.N. projects to areas 11 and 12 (old Brodman scheme) in the orbital region of the frontal lobe. The medial part of the parvicellular nucleus of the D.M.N. projects to area 11 and probably 47. Glees, Meyer and Meyer (1946) have shown that afferent fibres to the frontal lobe terminate in the third and fourth layer of the frontal cortex which are considered to be the main cortical receptive layers. The dorsolateral part of the small celled portion is connected with area 45 and 46 and the ventrolateral part with area 8. The central part of the D.M.N. projects to areas 9 and 10 and perhaps 6. In other words the central part of the D.M.N. is connected with the frontal pole, the lateral portion with the convexity and the medial portion with the orbital surface.

The function of these connections is not yet clearly defined, but it can be considered as established that the D.M.N. is essentially a relay station for impulses coming from the hypothalamus. Clark and Boggon (1933) did show that fibres from different parts of the hypothalamus reach the magnocellular part of the D.M.N. This has recently been confirmed by Murphy and Gellhorn (1945) in physiological neuronographic studies. They claim to have found connection of the hypothalamus to the D.M.N., the D.M.N. to the cortex and the cortex to the D.M.N. and hypothalamus (Fig. 2). As the D.M.N. is also fired by stimulation of the ventrolateral nuclear group of the thalamus a modification of the impulses from the hypothalamus may result. The impulses from
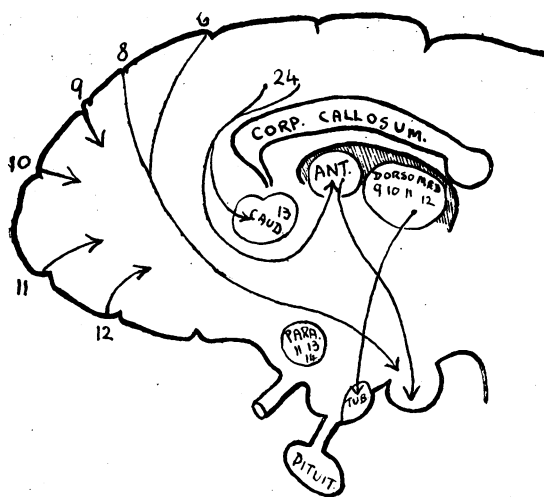
FIG. 2.—Diagram showing cortico-thalamic and cortico-hypothalamic connections.

the D.M.N. to the cortex are, therefore, not only the result of hypothalmic activity but also of some additional activity of the thalamus itself (Le Gros Clark, 1948).

Connections of the Anterior Nucleus of the Thalamus (N.A.M.)

Le Gros Clark (1933) and Lashley (1941) found that lesions in the anterior part of the cingulate gyrus (area 24) lead to degeneration in the medial half of the N.A.M. If the lesion is more caudal in the cingulate gyrus the lateral half of the N.A.M. degenerates. Meyer and Beck (1947) found that area 24 receives fibres from the antero-medial part of the nucleus anterior medialis. This nucleus is of special interest as it is also the terminal station of the mammillothalamic tract conveying impulses from the mammillary body in the hypothalamus. The mammillary bodies receive the efferent fibres from the whole hippocampus via the fornix. Areas 24 and 23 are, therefore, mainly projection areas of the hippocampus with relay stations in the mammillary bodies and the N.A.M. The significance of this projection is still doubtful.

Connections of Other Thalamic Nuclei with the Frontal Lobe

For the connections of other thalamic nuclei with the frontal lobes there is no anatomical evidence. Morrison and Dempsey (1942) could show, however, that stimulation near the medial medullary lamina of the thalamus produced changes in the electrocorticogram in all parts of the cortex. They also found a point to point relationship of the D.M.N. to specific areas in the

frontal cortex and, therefore, believe that there is one specific system with a point to point arrangement and a non-specific system with diffuse connections.

Efferent Connections of the Frontal Lobe

Corticostriate fibres connect the suppressor areas of the frontal cortex with the caudate nucleus (Carol and McCulloch, 1944). These fibres form part of a circuit mediating suppressor functions via the thalamus and hypothalamus. Cortico-thalamic fibres descend from the frontal areas to the D.M.N. These connections are claimed by Murphy and Gellhorn (1945) by electroneurono-graphic methods. Le Gros Clark also found these connections in lower animals with the Marchi method. Freudenberg, Glees and Obrador (1947) could show that fibres from the D.M.N. to the frontal cortex take a slightly different course than the efferent fibres from the frontal lobe to the thalamus. McCulloch recently found cortico-hypothalamic fibres by physiological neurono-graphy. Connections exist between specific cortical areas and the supraoptic, paraventricular and posterior hypothalamic nuclei and also the mammillary body. The supraoptic nuclei are connected with the pituitary by non-myelinated fibres. Cortico-tegmental fibres connect the frontal lobe with the tegmentum of the midbrain.

Conclusion

It is of great interest that changes seen in patients after leucotomy have confirmed many of the physiological findings mentioned above as, for instance the results of Dax and Radley Smith (1946) showing that the low vertical cut is best avoided in aggressive and paranoid schizophrenics, as lesions interrupting projection fibres to area 13 and 14 may lead to an increase in aggressiveness. The effects of orbital leucotomies described by Reitman (1946) as euphoria, extraversion and hyperactivity, are also related to the functions of the orbital cortex as good responses were seen to follow symptoms of introversion, emotional dulling, blockage of thought and depersonalization. The improvement of these symptoms is possibly related to the hyperactivity seen after lesions to area 13 and 14. In aggressive chronic schizophrenics the best results seem to have been obtained by massive severance of the white matter (lobotomies) which seems to agree with the observations in leucotomized monkeys (Freudenberg, Glees and Obrador, 1947).

Surgical Aspects

Destruction of the white matter of the frontal lobes by surgical operation in the treatment of mental illness was first performed only 12 years

ago, in 1936, by Moniz and Lima. Since that time many different techniques have been employed in all parts of the world and already ablation of various portions of the pre-frontal grey matter has been tried in place of division of the white matter, but division of varying proportions of the white matter is still the standard operation. In this section we shall use the term *lobotomy* to denote a wide or sub-total division of the white matter and *leucotomy* when a comparatively small and selected portion only is divided.

Approach

Surgical approach to the frontal white matter has been made from above (Duff, 1946), from below through the roof of the orbit (Fiamberti, 1937) and more commonly from the convex lateral surface (Freeman and Watts, 1942) or through the temporal fossa (Dax and Radley-Smith, 1943). In general, the plane of division of the fibres lies just anterior to the tip of the anterior horn of the lateral ventricle—' the critical plane of section' of Freeman and Watts, but other sites have been used (Obrador, 1947). Usually, access to the frontal lobes has been gained by making a small trephine or burr-hole in the skull on both sides but some operators have made a wide exposure of the brain by turning an osteo-plastic flap or flaps. Such major surgical procedures are only justifiable if they lead to appreciably greater accuracy of localization or to more certain prevention of haemorrhage.

Method of Destruction of White Matter

The white matter has been destroyed in a wide variety of ways—by the injection of alcohol as a chemical coagulant and by surgical instruments. Many surgeons employ well-known instruments originally designed for other purposes—the brain-needle, the blunt dissector without modification or modified as by Harvey Jackson who uses one curved ' on the flat ' like a scimitar to facilitate the division of the uppermost and lowest fibres. Others have devised special instruments for this purpose—the ' leucotome' in its many forms. The MacGregor leucotome has, at that end of the shaft which is inserted into the brain, a blade which is caused to rotate through a circle by the turning of a screw fitted to the handle or external extremity. The length of shaft inserted into the brain can be controlled by a moveable guard which is set on a centimetre scale. The blade when closed for insertion or withdrawal lies in the hollow shaft of the instrument, the lumen communicates with a side tube brought out along the handle through which C.S.F. will drip if the blade enters the lateral ventricle. The blade has a blunt edge

to avoid division of blood vessels. This instrument has been further adapted to provide greater delicacy of feeling by the provision of a screw which has to turn through four complete revolutions in order to turn the blade over once in the brain. In this way it is possible to feel the resistance of a cerebral vessel (Fig. 3). The very justified fear of damaging cerebral vessels led MacGregor in 1942 to devise an expanding wire loop which may well push before it, rather than divide, any vessels it may chance to encounter in the brain, but it may also compress rather than sever the nerve fibres.

Type of Incision

The division of white matter, in whatsoever vertical plane may be chosen, may vary from an attempted complete division to a localized section of some only of the fibres. The employment of small cuts in different parts of the vertical plane in the treatment of the various symptom-complexes —selective leucotomy—has been described by Freeman and Watts, 1942 ; McKissock, 1943 ; Smolik, Hoffstetter and Busch, 1945 ; and Dax and Radley-Smith in 1943 and 1946. Good results have especially been claimed for those low vertical sections which divide the fibres arising from the orbital or ' emotional' cortex (orbital cut). In 1943 the writers described a horizontal leucotomy in which the plane of section lies parallel to and just above the orbital cortex.

It may be helpful to describe in rather more detail the operation which has been evolved at Netherne over a period of some six years and to record the surgical experience of some 300 cases.

Anaesthetic

The operation of leucotomy can, *per se*, be suitably performed under local anaesthesia if the patient is co-operative, but this is often not the case and, therefore, general anaesthesia has been most commonly employed. Light general anaesthesia as by pentothal induction followed by intra-tracheal gas and oxygen with perhaps a little trilene or ether has proved satisfactory. Vessels divided in the plane of section cannot be coagulated and, therefore, it is desirable to avoid any post-operative restlessness. Intramuscular luminal (3 gr.) is given before the end of the anaesthetic, and on return to bed the patient receives a rectal injection of aspirin, bromide and chloral, repeated often two or three times in the first day.

Position

The patient lies supine with the occiput supported in a sorbo rubber ring pad. The table is tilted to bring the head appreciably higher than the rest of the body which serves to minimize

cerebral congestion. By tilting the table from side to side the operation is facilitated as the side of the head being operated upon may be placed in an almost horizontal plane.

Skin Preparation

Despite the obvious disadvantages, expecially in women, it is considered wise to shave the whole head. In very disturbed patients this step occasionally presents a major problem which may require the administration of an anaesthetic or an electrically-induced convulsion on the day before operation. After the previously shaved head has been repurified on the operating table it is covered with a sterile ' hood ' having two holes, one over each temporal fossa.

Operative Technique

A skin incision with its centre upon a point 3 cm. behind the outer border of the orbit and 3 cm. above the zygoma is made sloping slightly forwards and this falls just within the hair margin. The bone is exposed by splitting and retracting the temporal fascia and muscle, and in it a burr or trephine hole is made which includes the junction of the coronal and squamosal sutures. The anterior branch of the middle meningeal artery usually crosses the exposed circle of dura and, indeed, it may be encountered in its bony canal at the lower end of the bony defect. The dura is opened and the vessels in the lower end of the Sylvian fissure sought, if necessary by slightly enlarging the aperture in the bone. It may be appropriate at this point to explain our choice of this skin and bone incision which is some 3 cm. lower than the classical surface marking. This lower exposure is so near the floor of the anterior fossa that it is impossible to be too low and the visualization of the Sylvian vessels prevents too high an incision and fixes the antero-posterior position. When the higher incisions were formerly employed the examination of post-operative and experimental cadaver brains convinced the writers that the lack of any easily recognizable point on the surface of the brain sometimes led to the incision in the brain being made where it was not intended to be—e.g. too far posterior. A stab incision is made in the pia-arachnoid at a point where an imaginary line 1 cm. above and parallel to the Sylvian vessels intersects a horizontal line just above the centre of the opening. The leucotome with its blade closed (ensheathed in the shaft) is inserted at this point. The depth of penetration is determined by the previously ascertained width of the brain which has been measured, after opening the skull on both sides, with a caliper of the pelvimeter type. The

leucotome is always inserted at the point described above, but the direction in which it is caused to point depends upon which fibres are to be sectioned. For the vertical leucotomies the instrument is inserted so that its blade in rotating cuts a vertically disposed circle of the fibres running backwards from the frontal cortex to the thalamus, but by pointing the leucotome at different points on a line drawn from the opposite zygoma to the vertex, fibres may be cut at a variety of levels in the vertical plane. Thus we describe an upper, middle and lower (or orbital) vertical cut (Fig. 4). Further, the blade of the leucotome is inserted to different depths in order to divide appropriate fibres. The circles of white matter cut in each of these incisions have been defined by experimental work on the brains of fresh cadavers, which has been described in more detail in the *British Journal of Surgery*. These incisions may be used singly, in pairs or in combination with the horizontal sections above the orbital cortex. It is the writers' impression that the leucotomy should be performed on both frontal lobes at the same operation, for where any complication has prevented the bilateral section the clinical improvement obtained has in some cases not been as satisfactory as was anticipated. If, perforce, the operation cannot be completed, the other side should be divided as soon as possible. Unilateral leucotomy is very rarely a success. The leucotomy is most carefully positioned and the side tube watched for an outflow of C.S.F. which would denote an accidental tapping of the anterior horn of the lateral ventricle necessitating a more anterior re-insertion before the blade is caused to rotate by turning the screw in the handle. This step of the operation should be taken most deliberately and carefully in order to feel the resistance of any large vessel which the revolving blade may meet. If such resistance is encountered the blade is turned back. In general the blade turns over and re-enters its sheath without any undue resistance being met, and the leucotome is then rotated back to its original position and withdrawn very slowly. On several occasions a deep cerebral vessel caught between the closed blade and its sheath has been withdrawn with the instrument in the form of an unsevered loop and this has thus been rendered amenable to coagulation or ligature before it is torn and retracts into the brain. When haemostatis has been secured the muscle and scalp are closed in layers with interrupted stitches.

On several occasions reoperation has been performed, perhaps when considerable temporary improvement has been obtained, but relapse has occurred. At the second operation a different section may be done—a horizontal or middle vertical following a previous low vertical.

Post-Operative Course

Post-operative restlessness is combated by appropriate sedatives. We regard such restlessness not only as dangerous but, if excessive, perhaps of bad prognostic import. A slight pyrexia usually lasts for 48 or 72 hours. The patients are kept in a recovery room adjacent to the theatre until the risk of immediate complications is over. Lethargy, confusion, disinclination to feed without persuasion or assistance, and incontinence are often described and to some degree are almost usual. We have found incontinence to be rare, and if present to be of short duration, after leucotomy, but lobotomy often produces incontinence for four or five weeks. The incontinence is probably due not so much to the damage of any essential part of the mechanism directly involved in the acts of micturition and defaecation as to the production of a post-operative mental state in which the patient cannot be bothered to call for a bed-pan or, when up, to walk to the lavatory. Such troubles presumably improve as the traumatic oedema of the brain around the cut subsides.

Recognizable changes in autonomic responses occur after operation and will be referred to elsewhere.

Complications

The only serious operative complication is haemorrhage into the substance of the brain or into the lateral ventricles arising from the injury of a deep cerebral vessel and the great majority of the early post-operative deaths have been due to this cause. Indeed it is difficult to see how the occasional damage of an unusually placed large, deep vessel is to be avoided as long as the present blind type of brain section is made. If the haemorrhage is diagnosed early the only effective treatment is likely to be a formal lobectomy with coagulation of all vessels in the cut surface of the brain. Such injury to deep vessels is of such transcending seriousness that all steps to prevent it should be taken and in the description of the operation such prophylactic measures have been indicated.

Mortality rates vary very widely from 1 or 2 per cent. up to 10 per cent. Bad risks may be excluded by one operator but accepted by another in an attempt to mitigate the lot of a tormented, agitated patient. Those series containing a high proportion of young and early cases should, other factors being equal, show a lower mortality than those including a high proportion of aged, arteriosclerotic and deteriorated patients.

Infection is extremely rare and, therefore, meningitis should barely warrant mention as a complication.

Damage to the basal ganglia may follow a too posterior section and such a case with transient rigidity, tremor, apraxia, etc., has been described by Reitman (1946).

Epileptic attacks sometimes occur after this operation as after other forms of cerebral injury. Major fits or brief attacks—petit mal type—have been described. The writers feel that leucotomy carries an appreciably lesser risk of epileptic manifestations than does lobotomy. The fits usually develop weeks or months after operation and vary in numbers from a single manifestation up to a dozen or so. There is some evidence that epilepsy is rarest of all after the lower or orbital cuts.

Leucotomy and lobotomy have now been performed in a sufficient number of cases and for a long enough time to provide a mass of post-mortem material comprising both early and late post-operative deaths where death occurring perhaps years after operation has been due to intercurrent diseases. Not infrequently in the late deaths a cyst of considerable size is found at the site of the medullary section. One supposes that an unusually large degree of bleeding has been responsible for the development of these cysts, but it is doubtful if it should be regarded as a complication since the clinical result has often been good.

The Future

It appears that for at least the immediate future some form of this operative treatment of mental illness will continue to be used and it is, therefore, of interest to speculate upon possible lines of development and improvement. A form of diathermy electrode which could be used to divide the white matter would be useful. Division of the white matter in toto or in part may give place entirely to ablation of areas of the prefrontal cortex. Already certain areas have been removed in series of cases—for instance areas 9, 10 and 46 together, and area 32, but to date the success of such methods is not established.

Clinical

The greatest difficulty experienced in assessing the clinical results of the operation and evaluating the complications and contraindications is the lack of uniformity in the recording of the findings by different workers. It is of obvious importance to know, for instance, whether the patients have been adequately treated by appropriate methods prior to operation, the technique which was used and the duration of illness; additionally, many of the recorded results refer to small numbers of cases before the writers have had the opportunity of acquiring experience in the details of the operation or the choice of suitable subjects. There are,

therefore, wide variations in the figures and divergent opinions as to the indications for the operation or the surgical method which should be employed.

With few exceptions it is generally agreed that leucotomy should not be undertaken until the other recognized forms of treatment have failed ; but the assessment of the adequacy of the previous treatment and even of the necessity for its use is inclined to vary.

The operation has been mainly performed upon melancholics, obsessionals and schizophrenics, but to quote Henderson and Gillespie, ' the tendency is to select patients for treatment more on a symptomatic than on a nosological basis.'

There is agreement that the severe obsessional neuroses, with rumination or compulsive actions sufficiently severe to produce a constant state of tension and to interfere with their day to day activities, are suitable cases for operation and can be expected to show a marked improvement in 70 to 90 per cent. of cases. We have, however, seen schizophrenics who have been relieved from their obsessional symptoms with a resulting exacerbation of their psychotic symptoms. It seems that in the obsessional-compulsive neuroses the underlying fear component is diminished by the operation so that the patient no longer has the need to be anxious if the acts are not performed, and in consequence they gradually disappear.

In melancholia a fairly accurate prognosis may also be given, but both Freeman and Watts' (1946) and the Board of Control's (1947) figures suggest that the chances of improvement diminish as the duration of illness increases. Depression and agitation as symptoms react very favourably to the operation and although a number of cases of suicide have been recorded following leucotomy the tendency towards it is markedly decreased even in cases who have not shown enough improvement to leave hospital. Good results have been claimed in from 50 to 90 per cent. of melancholics, but when there are so many remissions with convulsion therapy it would seem indefensible to subject a patient to leucotomy without first using this other form of treatment. The involutional psychoses have reacted very well to the operation and over 80 per cent. of Freeman and Watts' cases have shown improvement.

To assess the value of the operation in schizophrenia is a more difficult matter. The chronic patients in mental hospitals are largely schizophrenics and they form the great majority of those who are difficult and disturbed. It is not, therefore, surprising that any new form of treatment should have its most extensive trials on these cases in order to attempt to improve their condition and for the sake of the staff looking after them. Although the reported results have in most cases concerned a condition labelled as schizophrenia it is obvious that a heterogeneous collection of material is covered by the diagnosis and the figures have to be correspondingly assessed. In the first place it appears that these cases can be divided into two groups. The first consists of those with ' conduct disorders,' often but not necessarily of long history, who may be violent, aggressive, impulsive, dirty or destructive. The second embraces the patients of better prognosis, assessed perhaps on Freeman and Watts' (1946) three criteria of emotional response—severity of complaints, disturbing behaviour and autonomic imbalance—or on Frank's (1946) criteria ; the type who had failed though they might have been expected to respond to the usual forms of treatment for schizophrenia. It appears that good and fair results may be very differently assessed in the two groups and have a definite effect upon the figures given. It would appear that in the past the first type of case has been more frequently operated upon in Britain than in the United States, and no less than 539 of the 1,000 cases in the Board of Control's report belonged to the violent and difficult groups. The discrepancy of the results is shown in that 20.8 per cent. of the 573 schizophrenics collected in the Board of Control's report had left hospital and only 26 per cent. of Freeman and Watts' first 96 cases remained in hospital (1947). In the schizophrenics collected from our own first 250 operations the percentage of the discharges for the second group were four times as high as for the first.

Another point of particular importance in the case of schizophrenics is the duration of the illness ; the chances of recovery after insulin treatment decline rapidly with the length of history, and it would appear from the figures that much the same is to be expected after leucotomy. In Freeman and Watts' cases 85 per cent. with a duration of illness of less than two years gave good results and only 31 per cent. of those with a longer history ; from the Board of Control's report 52 per cent. of the schizophrenics with less than two years' history and 20 per cent. of those with two to four years' history were discharged as recovered or improved.

In either case, whether the operation is performed for conduct disorders or with a fair expectation of recovery, the figures suggest that it is well worth while using providing the cases are carefully chosen, but as Freeman and Watts (1946) say, ' a deteriorated schizophrenic looks and acts about the same with or without his frontal lobes ' and these cases are very rarely worth doing. It has also to be borne in mind that
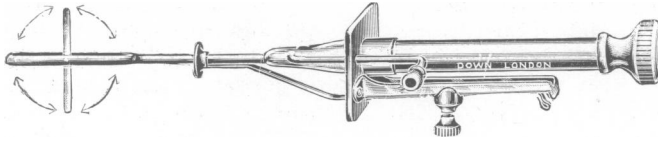
FIG. 3.—Leucotome (Down Bros.).

some emotional release may sometimes be expected, particularly after sections above the orbital cortex (Reitman, 1946), so that unless the operation is planned to the patient's symptomatology, it may intensify rather than diminish his disturbed state and even result in his becoming homicidal.

As an extension of the results gained in these disturbed patients, the operation has been used for epileptics, post-encephalitics, mental defectives with gross conduct disorders and delinquents. The results have been very variable but some improvements have been claimed ; though with the exception of the epileptics only small series are involved and no conclusions can be drawn.

An interesting and important indication for leucotomy was reported by Freeman and Watts (1946) who described the alleviation of painful states which had resisted other procedures. They believed the effect to be due to the removal of the emotional component and they and others have described some striking successes in apparently hopelessly incurable conditions.

In general it may be said that if the results of all the leucotomy operations were collected it might perhaps be expected that very roughly a third would be good, a third fair and a third poor, but these figures are of little real use. In chosen cases who have failed to react to other forms of treatment but with a good pre-psychotic personality and other favourable features, there still remains at least a two-thirds chance of the results of operation being good whatever their diagnosis, providing they show the type of symptomatology which reacts to the operation. Patients with less than two years' history give many more good results than those in whom the illness has lasted longer ; there is some evidence that males do better than females though this is not very definite. Older patients have shown better results than younger probably because the involutional affective states are included in the upper range and the schizophrenics of poor prognosis in the lower.

The mortality rate is found to be about 3 per cent. as calculated from five of the largest series of cases totalling 2,500 operations ; the majority of the deaths are due to cerebral haemorrhage.

The physical complications of the operation may be divided into immediate and remote. Soon after operation death has been caused by cerebral haemorrhage, post-operative pneumonia or anaesthetic complications. Urinary incontinence commonly occurs, but it appears to be much more frequently found and to last for longer in subtotal rather than localized sections of the white matter ; it rarely persists.

Of the remote physical complications epilepsy is of the greatest importance and frequently occurs three to nine months after the operation. With
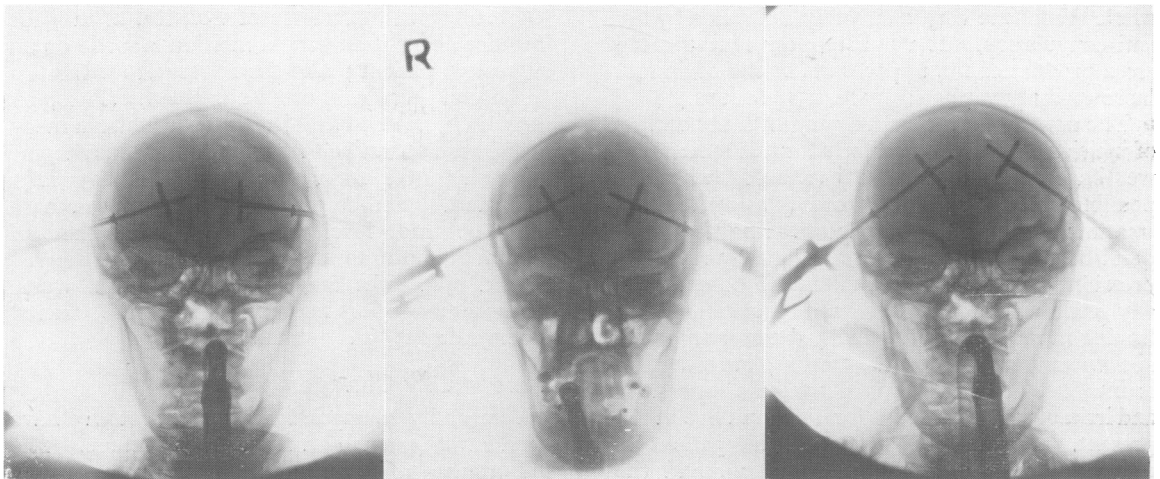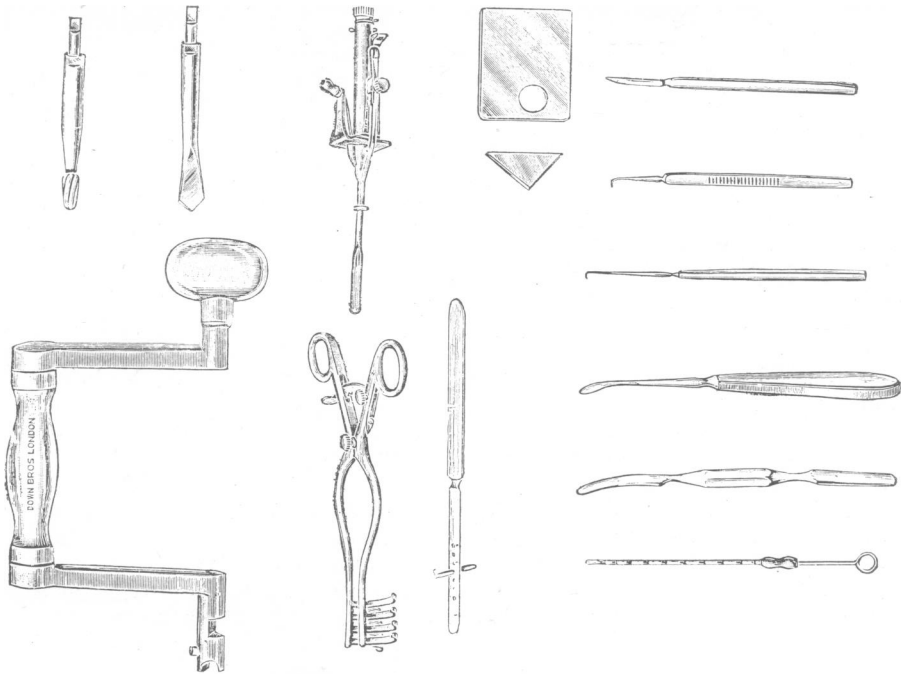

FIG. 4.—Illustrating a lower (or orbital), middle and upper vertical cut. X-rays of the leucotome in position.

LEUCOTOMY INSTRUMENTS

On the left is a brace and bits for drilling the holes in the skull. In the middle of the plate below there is a mastoid retractor for holding the skin and muscles back, beside it is an instrument with an adjustable crosspiece sometimes used for cutting the brain in the operation. Above the mastoid retractor is a leucotome, the blade at its lower end is rotated by turning the screw at the top. Beside this there are two plates for measuring the position of the skull opening. The instruments on the right of the plate are mainly for opening the membranes covering the brain. (*Reproduced by permission of the publishers, Messrs. Faber and Faber, from 'Modern Mental Treatment' : A Handbook for Nurses by E. Cunningham Dax*).

lobotomy the frequency is often as high as 10 per cent. ; with leucotomy it is much less and with orbital leucotomy it has never been reported. Status epilepticus occasionally occurs but on the whole the fits are very adequately controlled by the anti-convulsants. It would appear that the fits are a product of the upper parts of the brain and more easily precipitated by massive lesions.

The mental complications vary with the variety of incision and it is particularly for this reason that we believe that leucotomy should, wherever possible, be preferred to lobotomy as a means of treatment. The typical symptomatology has been described after the larger operations by such expressions as these :—Patients tend to be emotionally shallow, easily influenced in mood and act, lacking in reticence, emotionally deteriorated, outspoken and buoyant, rude, tactless, introspection is impossible, they lack initiative, are egocentric and irritable, have defective foresight and live in the present. Fortunately, however, the patient is usually capable of much re-education, and the care given in the months following operation is one of the most important features in determining

its success and counteracting the unpleasant symptoms of the post-operative state.

Hutton (1947) has called attention to some contraindications. The greatest care must be taken to avoid the release of violence, as may for instance occur if an orbital incision is made on an aggressive patient ; also the release of restraint in an asocial person must be avoided. Thus, by careful choice of the subject and the incision many of the post-operative mental complications may be avoided. In a number of cases, however, the maximum possible incision, perhaps even at a more posterior level than ' the critical plane of section ' appears to be the only means of relieving certain symptoms and this may be well worth while, although it is known that a definite ' frontal lobe syndrome ' may result.

Personality Changes

Personality changes following leucotomy have been investigated by a number of authors. The importance of their findings is dual ; first, they may determine the desirability or undesirability of the operation and, secondly, they may throw light

on the functions of the frontal lobe. Hunt (1942) in Freeman's monograph reported on very slight and not markedly significant alterations on the Rorschach test. Other psychometrists (Halstead, 1946) confirmed these findings.

Observations which were aimed at the assessment of post-operative personality modifications, based on the patient's behaviour, were more fruitful. In this connection Freeman's original concept was that the lobotomy resulted in the bleaching of the affect attached to the ego and that the post-operative attitudinal differences were sequels to the resulting emotional alterations. Kisker (1945) also believes in an emotional re-channelling and agrees in a broad sense with Freeman's concept of the moderate post-operative emotional detachment. Hutton (1942) emphasized the post-operative loss of final evaluation, that is to say the patients live in a perpetual present, thus confirming Fulton's observations on animals (vide supra). Golla (1946) reported that the moral and religious values of post-operative cases are impaired as they ceased to take any interest in religious patterns, and Malone (1947) elaborated the religious and moral problems in connection with leucotomy. Reitman (1947) described personality changes, confirming the altered moral attitudes and adding changed transference and financial attitudes, body image alterations, a sudden outburst of creative activity (also observed by Hutton and Bassett), and behaviour changes. He evaluated these findings as partly regressive and partly reintegrative phenomena.

These observations of various workers suggest that the post-operative changes can be evaluated either on the grounds of altered emotional re-channelling (Freeman, Kisker) or in terms of cognitive changes (Hutton, Reitman). The latter author devised a test which, by measuring alterations of conceptual thinking, gives an indication for post-operative cognitive disturbances. Cobb (1946) by favouring the theory of lowered cognitive functions expressed grave concern as to who should be leucotomized, advocating that this method of treatment should be reserved for elderly people only, with the forewarning that they might become a bit ' silly.' On the other hand Garmany (1948) does not believe that any personality changes can be observed which are attributable to the operation, thus differing from all the quoted authors.

The second set of problems arising as the result of the personality changes which have been found are connected with frontal lobe function. This is an entirely speculative matter, but as it has significant clinical bearings it should be discussed briefly. The original animal experiments of Jacobsen (1937) showed that sub-total extirpa-

tion of the prefrontal lobes caused reduction of the memory span, but not of intellectual function. Most important, however, in the light of Moniz's first operation was Jacobsen's observation that frustration did not induce rage reaction in the otherwise excitable chimpanzee. The alterations Jacobsen noted were related not to pre-operative normal but to abnormal neurotic behaviour. The dynamic neurological approach of the British school of neurology always emphasized that it is dysfunction which can be related to structural damage and not function. Neither Jacobsen's chimpanzee nor Brickner's classical case, nor indeed the greater proportion of psychotics and severe neurotics operated upon have had sufficiently intact pre-operative personality to enable the observers to draw conclusions about the functions of the normal prefrontal lobes and hence the results appear to be speculative.

Freeman and several others look upon the frontal lobes as concerned with foresight, or as Freeman expressed it in a recent paper (1948) with ' creative phantasy.' R. Russel (1947) thinks that the control and development of emotional reactions are the functions of the prefrontal lobes and that they mould the behaviour responses of the dominant parieto-temporal region. Such attempts at localization would lead us back to Kleist's outdated localization of cerebral function.

Cobb evaluates the post-operative personality changes as expressions of ' short circuiting,' and this Sherringtonian concept of brain functions attributes associative functions to the prefrontal lobes. Le Gros Clark, however (1948), drew attention to the anatomical evidence supporting the prefrontal lobes as being mainly projection areas. It may be important that our clinical results should be re-examined from Le Gros Clark's point of view, that is by looking upon the symptoms produced as due to disturbances of a deceptive nature rather than deficits in the sphere of association. Furthermore, since the electro-physiological work by Dusser de Barenne and his collaborators, direct corticohypothalamic tracts have been discovered. It might well be that the post-operative personality changes are merely phenomena of altered emotional expression, confirming Masserman's experimental studies on animals. Thus it is by no means settled whether the post-operative changes can be evaluated on Sherrington's ' short circuiting ' concept.

Conclusion

Lately Moniz re-emphasized his original conception of the hypothetical basis of leucotomy operation. He believes that in psychoses there is a fixed pattern of psychic activity, being in relation

E

to the stabilized synoptic pattern of activity in the brain. Moniz thinks that through leucotomy the patterns of psychic activity are altered through altering the neuronal pathways, but there is no experimental support for this hypothesis at present.

It appears that there is something to be said for evaluating the changes on the basis of the symptomatology produced by leucotomy, which superimposed on the pre-existing symptomatology covers up certain morbid expressions. In this connection the quantitative difference between leucotomy and lobotomy is important and the former would induce less symptoms than the latter. Furthermore, as was described above by the triad of extraversion, hyperactivity and euphoria produced by orbital leucotomy incisions, the location of the lesion may also be important.

In conclusion it would appear that the operation of prefrontal leucotomy, whatever may be its future, has opened a new approach to psychiatry and has produced some results which have never been previously obtainable. Its various techniques, clinical indications and its therapeutic value have been shortly reviewed and its importance as an instrument of research has been emphasized, but it should be borne in mind that this operation as a treatment is a symptomatic one resulting in a permanent impairment of some of the higher mental functions ; it also results in a lasting damage of some of the frontal areas. Whether it should remain in psychological medicine as a therapeutic means will depend on the research which one day may offer a better aetiological, hence therapeutic, approach for mental diseases.

BIBLIOGRAPHY

BAILEY, P., and SWEET, W. H. (1940), *J. Neurophysiol,* 3, 276.
BAILEY, P., VON VONIN, G., DAVIS, E. W., GAROL, H. W., McCULLOCH, W. S., ROSEMAN, E., and SILVEIRA, A. (1944), *J. Neurophysiol.,* 3, 51.
BOARD OF CONTROL (1947), Report on Prefrontal Leucotomy in 1,000 cases.
COBB, S. (1946), ' Borderlands of Psychiatry,' Cambridge.
DAX, E. C. (1947), ' Modern Mental Treatment,' Faber and Faber, London.
DAX, E. C., and RADLEY-SMITH, E. J. (1943), *J. Ment. Sci.,* 89, 182.
DAX, E. C., and RADLEY-SMITH, E. J. (1946), *Proc. R. Soc. Med.,* 32, 448.
DUFF, C. S. (1946), *Lancet,* 2, 639.

FIAMBERTI, A. M. (1937), *Ressegna di Studi Psichiat.,* 26(2), 797.
FRANK, J. (1946), *J. Ment. Sci.,* 89, 174.
FREEMAN, W., and WATTS, J. W. (1942) ' Psychosurgery,' Charles C. Thomas, Baltimore.
FREEMAN, W., and WATTS, J. W. (1946), *Am. J. Ment. Sci.,* 1, 1.
FREEMAN, W., and WATTS, J. W. (1946), *Proc. R. Soc. Med.,* 39, 445.
FREEMAN, W., and WATTS, J. W. (1947), *J. Comp. Neurol.,* 86, 65.
FREUDENBERG, R., GLEES, P., OBRADOR, S., FOX, B., and WILLIAMS, G. (1947), ' Demonstration at International Congress Physiol.,' Oxford.
FULTON, J., and INGRAM, F. D. (1929), *J. Physiol.,* 67, 27.
FULTON, J. (1943), ' Physiol. of the Nerv. System,' Oxford University Press.
GARMANY, G. (1948), *J. Ment. Sci.,* 94, 428.
GLEES, P., MEYER, A., and MEYER, M. (1946), *J. Anatomy,* 80, 101.
GOLLA, F. L. (1946), *Proc. R. Soc. Med.,* 39, 442.
GRENVILLE, G. D., and LAST, S. L. (1947), *Proc. R. Soc. Med.,* 40, 145.
HALSTEAD, W., CARMICHAEL, H., and BUCY, P. (1946), *Amer. J. Psychiat.,* 103, 217.
HEMPHILL, R. E., McLEOD, L. D., and REISS, M. (1942), *J. Ment. Sci.,* 88, 554.
HUTTON, E. L. (1947), *J. Ment. Sci.,* 93, 333.
HUTTON, E. L. (1947), *J. Ment. Sci.,* 93, 31.
JACOBSON, C. F., and ELDER, J. H. (1936), *Comp. Psych. Monograph,* 13, 61.
KISKER, G. (1945), *J. Gen. Psychol.,* 33, 171.
LE GROS CLARK, W. E. (1932), *Philos. Trans.,* 222, 1.
LE GROS CLARK, W. E., and BOGGON, R. H. (1933), *Brain,* 56, 83.
LE GROS CLARK, W. E. (1948), *Lancet,* 1, 353.
MacGREGOR, J. S., and CRUMBIE, J. R. (1942), *J. Ment. Sci.,* 88, 534.
MALONE, J. P. (1947), *Irish J. Med. Sci.,* 261, 573.
McKISSOCK, W. (1943), quoted by Fleming, *J. Ment. Sci.,* 1944, 90, 486.
METTLER, F. A. (1947), *J. Comp. Neurol.,* 86, 95.
MEYER, A., and McLARDY, T. (1947), *Proc. R. Soc. Med.,* 40, 141.
MEYER, A., BECK, E., McLARDY, T. (1947), *Brain,* 70, 18.
MONIZ, E., and LIMA, A. (1936), *Lisbon Med.,* 13, 152.
MORRISON, R. S., and DEMPSEY, E. W. (1942), *Amer. J. Physiol.,* 135, 281.
MURPHY, J. P., and GELLHORN, E. (1945), *J. Neurophysiol.,* 8, 431.
NICHOLS, I. C., and HUNT, J. McV. (1940), *Am. J. Psychiat.,* 96, 1063.
OBRADOR, S. (1947), ' Las Modernas Intervenciones Quirurgicas en Psiquitria.'
REITMAN, F. (1945), *J. Ment. Sci.,* 91, 318.
REITMAN, F. (1946), *B.M.J.,* 1, 235.
REITMAN, F. (1946), *Amer. J. Psychiat.,* 103, 2.
REITMAN, F. (1947), *J. Ment. Sci.,* 93, 55.
REITMAN, F. (1947), *J. Nerv. Ment. Dis.,* 105, 582.
RINKEL, M., GREENBLATT, M., COON, G. P., and SOLOMON, H. G. (1947), *Arch. Neurol. Psychiat.,* 58, 570.
RUCH, T. C., and SHENKIN, H. H. (1943), quoted by Fulton, J., 'Physiol. of Nerv. System,' 1943, Oxford University Press.
SMOLIK, E. A., HOFFSTETTER, L., and BUSCH, A. K. (1945), *Arch. Neurol. Psychiat.,* 53, 125.
VON BONIN, G. (1941), *J. Comp. Neurol.,* 75, 287.
WALKER, A. E. (1940), *J. Comp. Neurol.,* 73, 59.
WALKER, A. E. (1948), ' The Primate Thalamus,' University Chicago Press.